

Project 9.5. Signaling of AXL receptor in cancer cells

Supervisor: Professor Marta Międzyńska / auxiliary supervisor Daria Zdżalik-Bielecka, PhD

Institute: International Institute of Molecular and Cell Biology in Warsaw

Laboratory: Laboratory of Cell Biology

WWW: <https://bit.ly/3seh0nd>

Background:

AXL is a tyrosine kinase receptor that upon activation by its GAS6 ligand regulates cell growth, survival, migration and invasion. Overexpression of AXL occurs in a wide variety of cancer types and is associated with increased invasiveness and metastasis, as well as resistance of cancer cells to anticancer therapies. In our previous studies, we identified the AXL receptor interactome (a set of proteins with which the receptor interacts) and discovered that AXL binds numerous proteins that regulate actin cytoskeleton dynamics. Through such interactions, activation of AXL receptor stimulates the formation of peripheral and circular membrane ruffles that promote macropinocytosis and ultimately lead to cell invasion (see our manuscript at <https://bit.ly/2QfEVpF> for more details). Macropinocytosis is a form of endocytosis that allows cells to take up large volumes of extracellular fluid and the compounds dissolved within it. The macromolecules taken up through this pathway can be an important source of nutrients that fuel cancer cell growth. It has been recently proposed that macropinocytosis may also contribute to resistance of cancer cells to chemotherapeutics. We found that proteins in the AXL interactome may be involved in nutrient uptake by macropinocytosis. Elucidating their mechanisms of action in AXL receptor signaling will be the goal of the proposed project.

Aim:

The goal of this project is to investigate the molecular mechanisms of AXL receptor signaling that regulates cancer cell growth. Specifically, we will investigate how the AXL receptor and its ligand GAS6 stimulate uptake of nutrients from the extracellular environment via macropinocytosis. We will also determine whether and how this phenomenon contributes to drug resistance of cancer cells and, consequently, to the growth of tumors despite the applied therapy.

Requirements:

- Master's degree in biology, biochemistry or related field,
- Eligibility for PhD studies in Poland,
- Solid understanding of the principles of molecular and cell biology,
- Previous experience in laboratory work and familiarity with basic molecular biology techniques,
- Written and spoken fluency in English,
- Good interpersonal skills and a collaborative attitude,

Contact: mmiaczynska@iimcb.gov.pl; dzdzalik@iimcb.gov.pl